
Dispensable role of Drosophila ortholog of LRRK2 kinase activity in survival of dopaminergic neurons.

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ABSTRACT: BACKGROUND: Parkinson's disease (PD) is the most prevalent incurable neurodegenerative movement disorder. Mutations in LRRK2 are associated with both autosomal dominant familial and sporadic forms of PD. LRRK2 encodes a large putative serine/threonine kinase with GTPase activity. Increased LRRK2 kinase activity plays a critical role in pathogenic LRRK2 mutant-induced neurodegeneration in vitro. Little is known about the physiological function of LRRK2. RESULTS: We have recently identified a Drosophila line with a P-element insertion in an ortholog gene of human LRRK2 (dLRRK). The insertion results in a truncated Drosophila LRRK variant with N-terminal 1290 amino acids but lacking C-terminal kinase domain. The homozygous mutant fly develops normally with normal life span as well as unchanged number and pattern of dopaminergic neurons. However, dLRRK mutant flies were selectively sensitive to hydrogen peroxide induced stress but not to paraquat, rotenone and beta-mercaptoethanol induced stresses. CONCLUSION: Our results indicate that inactivation of dLRRK kinase activity is not essential for fly development and suggest that inhibition of LRRK activity may serve as a potential treatment of PD. However, dLRRK kinase activity likely plays a role in protecting against oxidative stress.

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